

**REMARKS**

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katsukiyo et al. (US Patent No. 5,733,892, cited in previous Office Action) in view of Shigehisa et al. (JP 06-072893, cited in previous Office Action).

Applicants respectfully submits that the present invention is not obvious over the cited art, and request that the Examiner reconsider and withdraw this rejection in view of the following remarks.

1. The joint injectable preparation of the present invention is considered to develop a joint protection function by a hydrogel having high viscoelasticity, i.e., a shock absorbing function. That is, this function differs from the suppression of cancer metastasis in Katsukiyo and the treatment of rheumatoid arthritis in Shigehisa in mechanism. Even though these prior art references mention an injectable preparation, the development of the disclosed effect can be expected if the injectable preparation is administered.

As understood from the passage "The amount of the active ingredient in the medical preparation may be varied within the range of from 1 to 90 % by weight based on the weight of the carrier" (column 36, lines 42-45) after a description of the preparation of Katsukiya cited by the Examiner (page 5, lines 11-14 of the present Office Action), the amount of the active ingredient may be 1 wt%. It can be understood from this that the disclosed pharmacological effect of the active ingredient is expected, and the injectable preparation is merely described as one of a large number of dosing preparations enumerated in Katsukiyo.

In contrast to this, the compound of the present invention must have a high elastic modulus (must be able to be administered) when it is prepared as a hydrogel and thereby can develop a joint protection function.

The present invention is a hyaluronic acid compound represented by the formula (1), that is, a combination of hyaluronic acid and phosphatidyl ethanolamine as set forth in claim 1. The desired object, that is, the protection of a joint can be attained by selecting a hyaluronic acid compound having numerical values specified in claim 1.

Both Katsukiyo and Shigehisa fail to disclose or suggest the above hyaluronic acid compound of the present invention and a joint protection function which is attained by the compound.

2. As the Examiner indicates, Katsukiyo does not disclose the embodiment of phosphatidyl ethanolamine where the acyl groups are unsaturated. Further, Katsukiyo also fails to disclose that a joint protection function is achieved by the hyaluronic acid compound of the present invention having the above embodiment.

3. Shigehisa discloses "hyaluronic acid, chondroitin, chondroitin sulfate (A, C, D, E, K), chondroitin polysulfate, dermatan sulfate, heparin, heparan sulfate, keratan sulfate, keratin polysulfate" as glycosaminoglycans (GAG) which are raw materials for the production of a lipid-bound glycosaminoglycan (paragraph (0020)) and also "phosphatidyl ethanolamine, phosphatidyl serine, phosphatidyl threonine, ethanolamine plasmagene, serine plasmagene, lysophosphatidyl choline, lysophosphatidyl inositol" as phospholipids out of lipids and teaches that "the chain length and unsaturation degree of the acyl group are not particularly limited but examples of the acyl group include palmitoyl (hexadecanoyl) and stearoyl (octadecanoyl)" as for the acyl group in the lipid. Further; examples of a reaction for producing the lipid-bound GAG

through bonding between the raw material GAG and a lipid include nine reactions (a) to (i) as described in the paragraph [0018].

The hyaluronic acid compound in claim 1 of the present application is obtained only by selecting hyaluronic acid as GAG and phosphatidyl ethanolamine as a lipid from the above raw materials enumerated in Shigehisa, further selecting an acyl group having an alkenyl group with 10 to 28 carbon atoms which is not described in Shigehisa and carrying out a reaction (e) out of the above reactions to bond these.

It is defined in claim 1 of the present application that the hyaluronic acid compound further has a group (formula (1)'-a) derived from phosphatidyl ethanolamine having an alkenyl group with 10 to 28 carbon atoms in the acyl group in an amount of 1 to 100 % of the total of all the carboxyl groups of hyaluronic acid.

When the above hyaluronic acid compound of the present invention has the above group represented by the formula (1)'-a in an amount of 1 to 100 % of the total of all the carboxyl groups of hyaluronic acid, it can form a hydrogel having a high elastic modulus of not less than 200 Pa and is useful for the treatment of a knee cartilage damage (see page 7, lines 18-21 of the present application).

Shigehisa teaches that lipid-bound GAG has the effect of suppressing the extension of pannus which causes cartilage destruction as an anti-rheumatic agent for improving the symptoms of rheumatism (RA) and the effect of easing the inflammation reaction of a synovial membrane and is used as an anti-rheumatic agent having little toxicity and few side-effects (see paragraph [0008]) but does not disclose that the lipid-bound GAG is effective for the treatment of cartilage damage of a joint such as a knee.

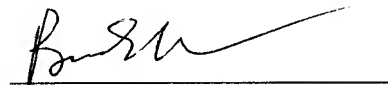
As described above, the hyaluronic acid compound in claim 1 of the present application is a novel compound having a specific structure which is not disclosed by Katsukiyo and Shigehisa and has an excellent function and effect, that is, a joint protection function and the effect of treating cartilage damage of a joint such as a knee which are not disclosed by Katsukiyo and Shigehisa.

Therefore, Applicants submit that the invention in claims 1-8 of the present application is not obvious over Katsukiyo in view of Shigehisa, and withdrawal of this rejection is respectfully requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

  
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